The reduction potential samples were prepared by adding tetraethylammonium tetrafluoroborate (0.217 mg, 1 mM) and the electron acceptor (in an amount calculated to give a final concentration of 2-4 mM) together in one cell, evacuating, flushing with argon 3 times, and then injecting Me_2SO (10 mL) from an argon flushed syringe.

Product Studies. The product studies were carried out by the method previously described using equivalent amounts of reactants.[1] Product isolations were effected by column chromatography. For example, the product from the reaction of 9-MeFl$^-$ ion and $PhSO_2CH_2Br$ was isolated by quenching with water, ether extraction, and adsorption on silica gel; elution with Et_2O/hexane (5/95) gave (9-MeFl)$_2$ as colorless crystals, identical by NMR with a known sample.[1] Elution with 10% Et_2O/hexane gave $PhSO_2CH_3$, mp 84 °C; identical by NMR and mmp with an authentic sample. The products formed from reactions with electron acceptors are summarized in Table IV.

Quenching the reaction mixture from 9-PhXn$^-$ ion and $Me_2C(SO_2Ph)_2$ gave a white solid, mp 219 °C dec, identified as (9-PhXnO)$_2$ by NMR: the reported mp is 219 °C.[20] The residue was adsorbed onto alumina. Elution with 2% Et_2O/hexane gave more (9-PhXnO)$_2$; elution with 20% Et_2O/hexane brought through Me_2CHSO_2Ph as a colorless liquid; mass spec (70 eV) m/e 184 (M^+), 141 (SO_2Ph); the NMR agreed with that previously reported.[21]

In the reactions with $PhSOCH_2Cl$ and Me_2CBr_2 with 9-MeFl$^-$ the dimer was isolated, but the products derived from the electron acceptors were intractable mixtures.

Acknowledgment. We are grateful to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the National Science Foundation for financial support.

Registry No. 9-(PhS)Fl$^-$, 71805-72-6; 9-(*p*-BrC_6H_4S)Fl$^-$, 73838-77-4; 2-Br-9-(PhS)Fl$^-$, 73838-76-3; 9-(*m*-ClC_6H_4)Fl$^-$, 73872-45-4; 9-MeFl$^-$, 31468-21-0; 2-Br-9-MeFl$^-$, 81255-42-7; 9-(*p*-$MeOC_6H_4$)Xn$^-$, 94929-75-6; 9-PhXn$^-$, 94929-76-7; 9-(*m*-ClC_6H_4)Xn$^-$, 85554-38-7; 2,7-Br_2-9-(PhS)Fl$^-$, 81245-84-3; 9-(CO_2Me)Fl$^-$, 12565-94-5; 2-Br-9-(CO_2Me)Fl$^-$, 73838-71-8; *p*-$MeC_6H_4C(Me)CN^-$, 94929-77-8; $PhC(Me)CN^-$, 56751-34-9; *p*-$ClC_6H_4C(Me)CN^-$, 85535-18-8; Ph_2CCN^-, 18802-83-0; 9-PhFl$^-$, 31468-22-1; $PhC(Me)SO_2Ph^-$, 85554-41-2; $Ph_2CSO_2Ph^-$, 85554-40-1; 9-*t*-BuFl$^-$, 73838-69-4; $PhSO_2CH(Ph)Br$, 15296-88-5; $PhSO_2C(Me)(Ph)Br$, 94929-78-9; Me_2CBr_2, 594-16-1; $PhS(O)CH_2Cl$, 7205-94-9; $Me_2C(SO_2Ph)_2$, 39863-09-7; c-$C_6H_{10}(NO_2)Ts$, 41774-12-3; $Me_2C(NO_2)Ts$, 21272-86-6; c-$C_6H_{10}(NO_2)_2$, 4028-15-3; $Me_2C(NO_2)Br$, 5447-97-2; $Ph_2I^+Cl^-$, 1483-72-3; $Me_2C(NO_2)_2$, 595-49-3; $PhSO_2CH_2I$, 65492-21-9; $PhSO_2CH_2Br$, 19169-90-5; c-$C_6H_{10}(NO_2)CN$, 58102-55-9; $ClCH_2SPh$, 7205-91-6; $PhSO_2Na$, 515-42-4; Br_2CH_2, 74-95-3; $PhCH(CH_3)SO_2Ph$, 24422-78-4; I_2CH_2, 75-11-6; *p*-$ClC_6H_4CH_2CN$, 140-53-4; *p*-$MeC_6H_4CH(CH_3)CN$, 75920-45-5; $CH_3CH(NO_2)CH_3$, 79-46-9; 2-Br-9-*t*-BuFl$^-$, 85535-33-7.

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Conformational Analysis, Synthesis, and Carbon-13 Spectroscopy of 9,9-Dimethylbicyclo[3.3.1]nonane Derivatives

Gérard Aranda, Jean-Marie Bernassau, Marcel Fetizon,* and Issam Hanna

Laboratoire de Synthèse Organique, Ecole Polytechnique, 91128 Palaiseau Cedex, France

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A series of 9,9-dimethylbicyclo[3.3.1]nonanes substituted in position 3 and/or 7 has been synthesized. Their conformational properties have been studied by force field calculations and ^{13}C NMR. These studies indicate that, in most of the compounds, the dimethyl bridge substitution forces the two cyclohexane rings in the chair conformation. The steric compression imposed on carbons 3 and 7 by this double chair conformation is found to displace their carbon-13 chemical shifts to high field.

Introduction

Compounds possessing the bicyclo[3.3.1]nonane skeleton have been the subject of numerous conformational and spectrometric studies.[1-11] Interest in these compounds arises from their twin cyclohexane structure giving rise to chair-boat interchanges and from the close spatial proximity of carbons 3 and 7, the endo substituents of which being able to initiate conformational changes or intramolecular transannular reactions.[5,11]

Naturally the conformation of the bicyclic skeleton depends on the size of the endo 3,7-substituents and most previous studies consider the chair to boat transformation as a result of the steric interaction of the endo substituents.

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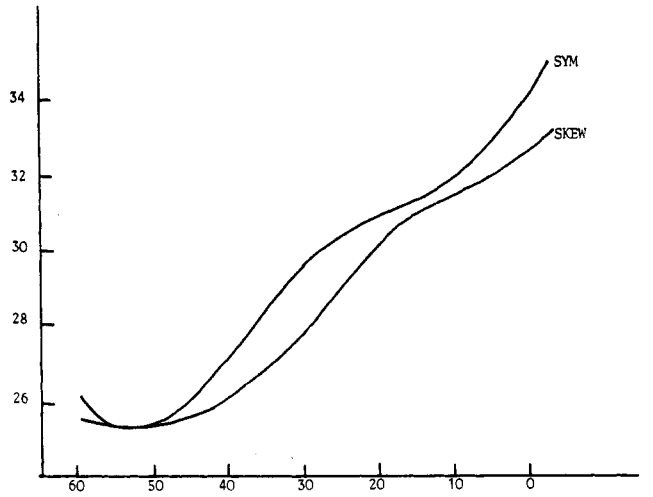


Figure 1. Energy of 9,9-dimethylbicyclo[3.3.1]nonane as a function of the 9–1–2–3 dihedral angle. The upper curve denotes conformations in which the 3–7–9 plane is a symmetry plane.

It seems therefore worth trying to separate these two conformational aspects, i.e., inhibiting the chair to boat interconversion and concentrating on the 3–7 interaction. Forcing the two cyclohexane rings in a chair conformation results in compounds in which the through space endo 3,7-substituents interaction can be maintained even under severe steric hindrance.

Introduction of a *gem*-dimethyl group at position 9 in the bicyclo[3.3.1] skeleton provides compounds with the aforementioned property since a boat cyclohexane ring possessing an axial methyl group presents unbearable steric constraints.

This paper describes the conformational properties, synthesis, and carbon-13 chemical shift analysis of a selected series of 9,9-dimethylbicyclo[3.3.1]nonane compounds possessing various substituents at positions 3 and/or 7.

Results and Discussion

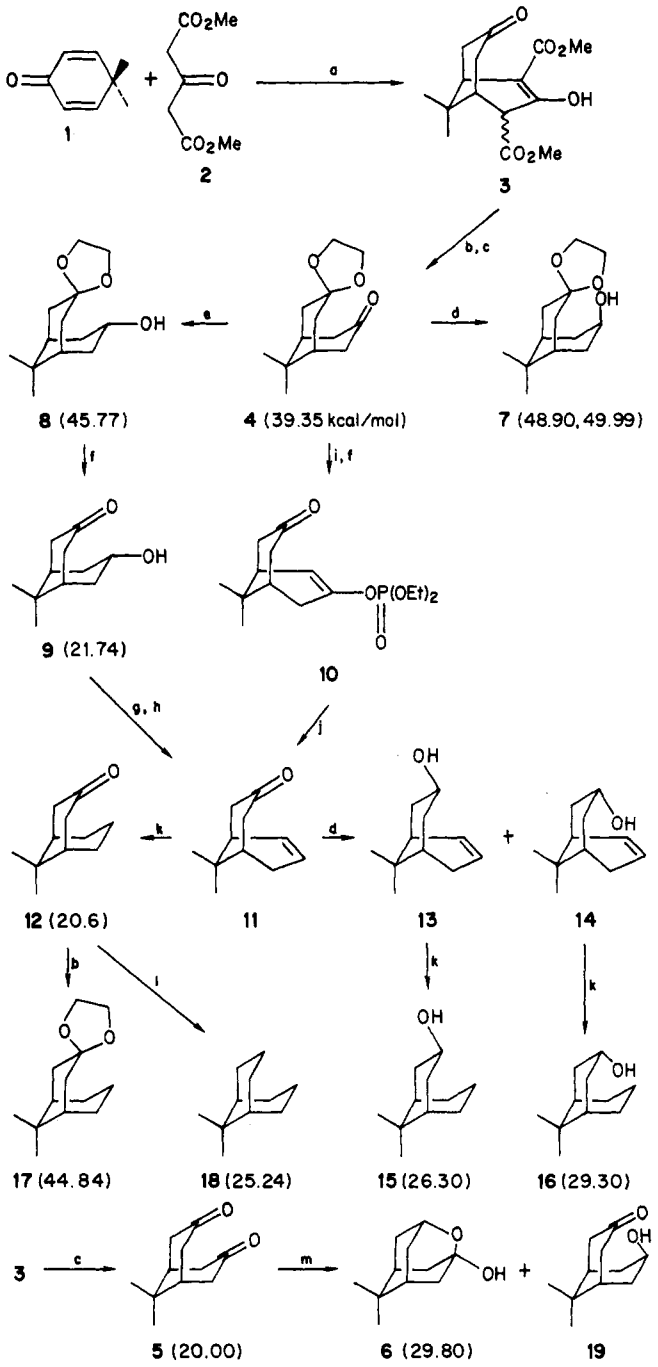
Force Field Calculations. As previously noted[4,6,7,10] compounds possessing the bicyclo[3.3.1]nonane skeleton can exist as four different conformations: chair–chair, chair–boat, boat–chair, and boat–boat. For bicyclo[3.3.1]nonane itself,[6] the most stable form is chair–chair, with the boat–chair and boat–boat conformations being higher in energy by 2.3 kcal/mol and 7.3 kcal/mol, respectively. When substituents are introduced at the endo 3- and/or 7-positions,[4,10] the conformer distribution varies, large substituents forcing the rings that bear them into the boat conformation.

When a *gem*-dimethyl group is introduced at position 9 computation with the MM2 force field shows that the boat form is no longer a stable conformation, i.e., only the chair–chair conformation exists. Figure 1 shows the energy profile when angle 9–1–2–3 is driven from 60° to −5°. At ca. 15°, the energy profile shows a marked flattening. This corresponds to a boat like conformation but is so destabilized by the 9-methyl group interaction that no local minimum is observed.

The through space van der Waals interaction of the endo atoms or groups of atoms bonded to carbons 3 and 7 is the main driving force of the conformational processes occurring in the bicyclo[3.3.1]nonane system. The molecule distorts itself so as to decrease this interaction to a reasonable value. This may occur through flattening of the cyclohexyl rings or partial skewing of each of them. This latter process destroys the planar symmetry of the molecule but, as the interconversion barrier between the two conformations is very small, this process cannot be disclosed by most physical methods and in particular ^{13}C NMR.

Selected compounds **4–9**, **12**, and **15–18** were subjected to a systematic MM2 calculation. For each compound, this involves eight different energy minimizations, starting from the four possible chair–boat combinations, with and without symmetry constraints across the 3–7–9 plane. Although symmetry constraints correspond to no physical reality in this system they were applied in order to see the benefits in energy strain obtained by skewing the molecule.

Scheme I[a]



[a] (a) MeONa, MeOH; (b) $(CH_2OH)_2$, C_6H_6, *p*-TSA; (c) NaOH, MeOH, H_2O; (d) $LiAlH_4$, THF; (e) Na, EtOH; (f) *p*-TSA, C_6H_6; (g) $ClC(S)OC_6H_4Me$, pyr; (h) 200 °C (0.5 torr); (i) LDA–THF then $ClP(=O)(OEt)_2$; (j) Li, $EtNH_2$, *t*-BuOH, THF; (k) H_2, Pd/C, EtOH; (l) Huong-Minlon reduction; (m) $NaBH_4$ (1 equiv), EtOH.

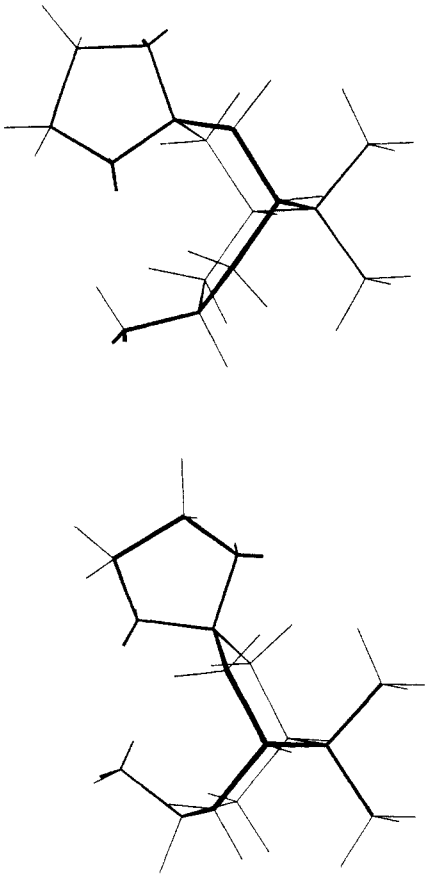


Figure 2. Conformations of 9,9-dimethylbicyclo[3.3.1]nonan-3-one ethylene acetal (**17**).

The lowest energies obtained for the 11 selected compounds are shown on Scheme I.

For all compounds except **7** a single chair–chair conformation can be assumed to be present in solution. If any of the nonchair conformations yielded a local minimum its energy was at least 10 kcal/mol higher than the chair–chair.

For all compounds, the nonsymmetric form is lower in energy. However the difference between symmetric and nonsymmetric is always very small (less than 0.1 kcal/mol). Thus in the chair–chair forms skewing is not a very favorable conformational process.

Comparison of **7** with **8** or **15** with **16** shows that introduction of an OH endo substituent raises the total steric energy of the molecule by ca. 3 kcal/mol. Without the 9,9-*gem*-dimethyl substituents the endo isomers would exist in the boat–chair form.[7] This is consistent with the force field calculations since conversion of one ring to a boat conformation is a more favorable process (2.3 kcal/mol) in the bicyclo[3.3.1]nonane series than in the *gem*-dimethyl series.

For compound **7** two conformations differing by 1 kcal/mol were found and are displayed in Figure 2. Both of them are of the form chair–flat boat. The conformation of lower energy is the one in which the cyclohexane ring that bears the alcohol is flattened. The preference of the molecule to flatten the cyclohexane ring bearing the alcohol could be due to the scissoring effect at carbon 3 (or 7). When the ring flattens the valence angle 2–3–4 decreases in value and thus the valence angle between geminal substituents at C(3) increases. When these geminal atoms are part of a five-membered ring, as in the ethylene ketal, internal constraints in the ring impede the scissoring effect.

The reliability of these calculations can be ascertained, to some extent, by comparison with X-ray data on similar structures. A rather sensitive test is the internuclear distance between carbons 3 and 7 or between the endo hydrogens they bear. This distance is found to be ca. 1.9 Å in the crystal[9] and ca. 2.0 Å from force field calculations.

Another interesting comparison, which tests for the effect of 9-substituents, can be made between 9-cyclohexylbicyclo[3.3.1]nonan-9-ol[9] and our compounds. From the point of view of the cyclohexane rings of the skeleton, the cyclohexyl 9-substituent has the same steric requirements as a methyl group, i.e., one hydrogen atom pointing toward the bicyclic structure. The dihedral angle 1–2–3–4, which is a good measure of the flattening of the nonskewed cyclohexyl rings, is found to be 39° by both X-ray data analysis and force field calculation. This value is similar to the one obtained in the bicyclic series without 9-substituents which shows that the geometry of the system is mainly controlled by the steric interaction between the endo substituents on the carbons 3 and 7.

A similar comparison can be made between the keto alcohol **9** and the corresponding compounds without the dimethyl substituents. In accordance with the X-ray structure,[5] the force field calculation reveals that the ring bearing the ketone is more flattened than the one bearing the hydroxyl. The dihedral angles involving the ketone are also satisfactorily reproduced (145° vs. 148° in the crystal) with the 77 force field whereas a previous study with the 72 force field did not reach such a good agreement.[5] One of main differences between the two force fields is in the torsional energy terms and it is thus not surprising that the improved 77 version yields better results.

The force field calculations are therefore found in good harmony with the X-ray data. This increases our confidence in them and puts the reactivity and spectroscopic interpretations on a firmer ground.

Synthesis. Scheme I outlines the synthetic routes used to prepare 9,9-dimethylbicyclo[3.3.1] derivatives.

Double Michael addition of 4,4-dimethylcyclohexadienone **1** with dimethyl acetonedicarboxylate **2** yielded the adduct **3** as a mixture of two fully enolized stereomers. Ketalization of **3** followed by decarboxylation of the crude product under basic conditions yielded the 9,9-dimethylbicyclo[3.3.1]nonane-3,7-dione 7-(ethylene acetal) (**4**). This approach has previously been used to construct bicyclo[3.3.1]nonane skeleton.[12]

Reduction of the ketone **4** proceeded in a highly stereospecific manner. The alcohol formed by *hydride reduction* ($LiAlH_4$ or $[(CH_3)_2CHCH_2]_2AlH$) was identified as the endo-3-ol **7** on the basis of its IR and ^1H NMR spectra. The course of the reaction can be rationalized in terms of approach of attacking reagent from the less hindered exo face of the molecule. On the other hand, reduction of **4** by *sodium in ethanol* gaves the exo epimer **8** as the sole product. No trace of **7** was observed. The assignment of exo stereochemistry relies on the ^1H NMR spectrum (the C*H*OH signal appears as a multiplet consisting of seven lines centered at δ 4.73[5]) and on the method of synthesis (the Na/EtOH reduction is expected to give the thermodynamically more stable alcohol[13]).

Hydrolysis of the ketal **8** gave the hydroxy ketone **9** which was acylated with *O*-4-methylphenyl chlorothioformate and the resulting thiocarbonate was converted into olefin **11** by pyrolysis[14] in 80% from **9**. More directly,

(12) For a review on synthesis of bicyclo[3.3.1]nonanes, see: Peters, J. A. *Synthesis* **1979**, 321.

(13) House, H. O. "Modern Synthetic Reactions", 2nd ed.; Benjamin, W. A., Inc.: Reading, MA, 1972; p 152.

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Table I. Carbon Chemical Shifts of 9,9-Dimethylbicyclo[3.3.1]nonane Derivatives

	C-1,C-5	C-2,C-4	C-3	C-6,C-8	C-7	C-9	others
18	37.4	27.9	21.1	27.9	21.1	30.3	27.9 (Me)
5	41.2	45.1	208.7	45.1	208.7	32.7	26.2 (Me)
6	38.5	31.5	93.8	38.5	71.4	34.0	26.4, 27.0 (Me)
4	38.2	43.3	209.7	37.1	107.4	32.6	26.6 (Me), 63.3, 64.2 (ketal)
7	38.5	31.6	71.4	36.1	96.2	34.4	26.4, 27.1 (Me), 62.4, 63.1 (ketal)
8	38.7	37.3	64.0	38.7	107.4	32.1	26.9 (Me), 62.4, 63.1 (ketal)
9	39.6	44.6	212.4	37.5	63.0	32.2	26.5 (Me)
12	39.2	44.5	213.4	28.1	16.6	32.5	26.4, 27.7 (Me)
15	38.7	38.1	66.6	27.1	20.6	32.2	26.8, 27.9 (Me)
16	36.7	37.0	62.4	27.6	15.5	31.8	26.8, 27.9 (Me)
17	37.9	39.7	108.1	27.6	15.4	32.1	26.8, 27.9 (Me), 63.1, 64.0 (ketal)

preparation of 11 was achieved from the ketone 4. Thus enol diethyl phosphate 10 prepared from 4 was reduced by lithium in ethylamine to give 11 in 50% overall yield.

While the hydroxy ketone 9 was readily obtainable, preparation of its 7-endo epimer 19 has not been a straightforward process. Attempts to prepare 19 by hydrolysis of 7 were unsuccessful. Thus overnight reflux of the ketal in a mixture of AcOH:H_2O 50:50 left the starting material unchanged. This lack of reactivity toward drastic chemical conditions confirms the high steric hindrance of this molecule.

In order to overcome this difficulty, preparation of 19 was devised from the diketone 5 which was obtained by decarboxylation of 3. Treatment of 5 by 1 equiv of sodium borohydride in ethanol gave a mixture of the desired product, 19, along with its internal hemiacetal 6. Formation of such an internal hemiacetal has already been reported[15] in the course of the reduction of a symmetrical cage dione.

The *exo*-3-ol 13 was obtained as a single product by reduction of 11 by sodium in ethanol, whereas lithium aluminum hydride gave a mixture of epimeric alcohols 13 and 14, easily separable by flash chromatography. In the ^{1}H NMR spectrum of 13 the C*H*OH signal appears at δ 4.00, again as a multiplet of seven lines. The assignment of exo and endo stereochemistry to 13 and 14, respectively, was confirmed by their reactivity toward catalytic hydrogenation. While the *exo*-ol 13 was readily saturated in a few minutes, complete hydrogenation of 14 necessitated an overnight reaction time.

Carbon-13 NMR. Assignments of the carbon-13 chemical shifts proceed straighforwardly from substituent effects and off resonance spectra. Deuterium exchange on ketone 4 allowed unambiguous assignments of the 2,4 and 6,8 carbon pairs of 7. Table I summarizes the carbon chemical shifts of some selected compounds.

The chemical shifts of these compounds follow the trends shown by similar compounds lacking the 9,9-dimethyl substitutions.[7] However, for the compounds presented in this paper, and except 7, no contribution of nonchair conformations can be called for.

A useful conformational probe of bicyclo[3.3.1]nonane is the 9-methylene and its chemical shift has been used to test for boat like conformations in the series.[4,10] With the *gem*-dimethyl substitution, this carbon looses its sensitivity to conformational charges and resonates consistently around 32 ppm. It is worth noting that this chemical shift is smaller than the value of the methylene of bicyclo[3.3.1]nonane itself (35.2 ppm).

Of special interest throughout these series is the influence of carbon 7 substitutions upon the chemical shift of carbon 3. As most of the compounds exist in a single chair–chair conformation, the chemical shift changes should be solely due to through space effects. Furthermore, would any conformational effects be present, like ring flattening or skewing, they would show up as chemical shift variations at positions 2 or 4. Inspection of the chemical shifts of compounds 12 and 15–18 shows that when an endo hydrogen is present at position 3, the chemical shift of carbon 7 is ca. 21 ppm. When no endo hydrogen is present carbon 7 appears shielded by 4–5 ppm. Meanwhile, carbons 6 and 8 consistently appear at ca. 27.5 ppm, indicating no conformational disturbance of the cyclohexyl moiety. The remote effect of an oxygen or a p orbital on a carbon-13 is therefore similar and shielding with respect of a hydrogen.

These steric carbon-13 chemical shift variations are thus found shielding in the compounds described here. This is not a general trend, as in the hibane series hydrogen and p orbital had similar effects shielding with respect of an sp^3 hybridized oxygen.[16]

Conclusion

Introduction of a *gem*-dimethyl group at position 9 in the bicyclo[3.3.1]nonane system inhibits the conformational transition of the cyclohexane rings from chair to boat. The carbons 3 and 7 are therefore maintained in close spatial proximity even when they bear bulky endo substituents.

Force field calculations indicate a unique chair–chair conformation except for the 3-ketal *endo*-7-OH compound in which one ring adopts a flattened boat conformation. In all the compounds the distance between endo 3,7-substituents remains at a similar value close to 2 Å.

The vicinity of centers 3 and 7 hampers reactant approach from the endo side of the molecule. Depending on the reaction this may lead to complete stereospecificity (4 to 7 or 8) or complete lack of reactivity (7 does not hydrolyze). It may also lead to intramolecular transannullar reactions as in the case of 6.

Finally, the proximity of the 3 endo substituent and the carbon 7 induces large chemical shift changes on that carbon. With respect to a hydrogen atom the effect of an sp^2 orbital or an oxygen atom at carbon 3 is a displacement of carbon 7 resonance ca. 5 ppm upfield.

Experimental Section

Melting points were taken on a Reichert or a Büchi 310 (sealed tube) apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 399 spectrometer as solutions in CCl_4. ^{1}H NMR spectra were recorded on Varian T.60 or Jeol PMX.60 spectrometers (60 MHz) as solutions in $CDCl_3$. ^{13}C NMR spectra were recorded on Varian CFT.20 (20 MHz) or XL.100 (25 MHz) apparatus. Mass spectra were recorded on a ZAB.2F Vg Micromass spectrometer. The force field calculations were done on

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an IBM 370/168 computer. Computation time ranged between 2 and 10 min for each conformation. The program used is an adapted version of MM2[17,18] providing simplified data entry and graphic output.

2,4-Dicarbomethoxy-9,9-dimethylbicyclo[3.3.1]nonane-3,7-dione (3). To a stirred solution of 0.5 g of sodium in 25 mL of absolute methanol was added a solution of 10.2 g (83 mmol) of 4,4-dimethylcyclohexadienone 1 in 50 mL of absolute methanol and 14.5 g (83 mmol) of dimethyl acetonedicarboxylate (2). The mixture was refluxed under argon for 21 h. A colorless solid which precipitated on cooling was collected, taken into chloroform, washed with 5% HCl, and then with water. Removal of the solvent left 13.0 g (53%) of fully enolized adduct 3 in the form of a mixture of stereomers. Recrystallization from methanol afforded colorless crystals: mp 148–154 °C; IR ($CHCl_3$) 3640, 3020, 1745, 1720, 1665, 1625 cm^{-1}; ^1H NMR δ 1.13 (s, 3 H), 1.33 (s, 3 H), 3.66 (s, 3 H), 3.68 (s, 3 H), 12.03 (s, enolic OH); ^{13}C NMR δ 25.7 (q), 26.1 (q), 33.4 (s), 39.1 (d), 40.9 (t), 42.0 (d), 42.6 (t), 49.5 (d), 52.0 (q), 52.1 (q), 102.8 (s), 165.7 (s), 170.5 (s), 171.8 (s), 208.5 (s). Anal. Calcd for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80. Found: C, 60.81; H, 6.77.

9,9-Dimethylbicyclo[3.3.1]nonane-3,7-dione 7-(Ethylene Acetal) (4). A solution of 3 (6.0 g), 80 mg of *p*-TSA, and 1.3 mL of 1,2-ethanediol in 200 mL of dry benzene was refluxed under argon atmosphere with a Dean–Stark trap for 8 h. The mixture was quenched with saturated $NaHCO_3$ solution and extracted with ether giving 7.2 g of colorless residue. A solution of this crude material and 2.5 g of NaOH in 100 mL of methanol and 100 mL of water was refluxed for 21 h under argon, cooled, acidified with 10% aqueous HCl, and stirred for 2 h until effervescence had ceased. The aqueous solution was exhaustively extracted with ethyl acetate to yield 2.84 g (62.5%) of colorless cristallized product. Recrystallization from pentane afforded 4 as colorless needles: mp 98–100 °C; MS 224 (16), 154 (100), 122 (84), 86 (52), 41 (38); IR: 1705 cm^{-1}; ^1H NMR δ 1.13 (s, 3 H), 1.18 (s, 3 H), 3.80 (s, 4 H). Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.34; H, 9.03.

Reduction of 4 with Sodium in Ethanol. 3-*exo*-ol 8. To a stirred solution of 4 (1.20 g) in 40 mL of absolute ethanol was added 2.50 g of sodium in small portions. The mixture was refluxed under argon atmosphere for 4 h, cooled, and poured into water. The product was extracted with ether to yield 1.22 g of oily product which crystallized on cooling. Recrystallization from pentane–ether afforded 8 as colorless needles: IR 1185, 3610 cm^{-1}; ^1H NMR δ 1.03 (s, 3 H), 1.10 (s, 3 H), 3.83 (m, 4 H), 4.73 (sept, 1 H). Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.75; H, 9.63.

Reduction of 4 with $LiAlH_4$. 3-*endo*-ol 7. To a stirred suspension of 350 mg of $LiAlH_4$ in 30 mL of THF was added dropwise a solution of 720 mg of 4 in 15 mL of THF under argon atmosphere. The mixture was refluxed for 90 min, cooled to room temperature, and then cooled in an ice–water bath. The excess hydride was destroyed by dropwise addition of 5% aqueous HCl. Extraction of the reaction mixture with ether gave 684 mg of oily colorless product homogeneous on TLC. Purification by flash chromatography yielded 7 as a colorless oil: IR 1175, 3450 cm^{-1}; ^1H NMR δ 1.08 (s, 6 H), 3.70 (m, 4 H), 4.20 (m, 1 H).

7-*exo*-Hydroxy-9,9-dimethylbicyclo[3.3.1]nonan-3-one (9). A mixture of 890 mg of hydroxy ketal 8 and 20 mL of acetic acid–water 30:70 was refluxed for 2.5 h. Neutralization with NaOH solution and extraction with ethyl acetate yielded 640 mg of colorless crystallized product. Recrystallization from methanol–ether afforded 9 as colorless needles: mp (sealed tube) 195–197 °C; IR 1705, 3610 cm^{-1}; ^1H NMR δ 1.20 (s, 3 H), 1.21 (s, 3 H), 3.65 (m, 1 H).

9,9-Dimethylbicyclo[3.3.1]non-5-en-3-one (11). A. From the Hydroxy Ketone 9. To a stirred solution of 9 (0.60 g) in dry pyridine (6 mL) cooled in an ice–water bath was added *p*-tolyl chlorothioformate (0.60 mL) under argon atmosphere. The mixture was stirred at room temperature for 3 h, poured into cold water, and extracted with benzene. The organic layer was washed with 5% aqueous HCl, water, and brine. The crude product was submitted to flash chromatography to yield 1.0 g of pure crystallized thiocarbonate: mp 165–167 °C; IR 1195, 1290, 1705 cm^{-1}; ^1H NMR δ 1.20 (s, 3 H), 1.26 (s, 3 H), 2.33 (s, 3 H), 5.30 (sept, 1 H), 7.00 (m, 4 H); ^{13}C NMR δ 20.9 (q), 26.3 (q), 26.5 (q), 32.3 (s), 32.8 (t), 39.5 (d), 44.2 (t), 7.72 (d), 121.6 (d), 130 (d), 136 (s), 151.3 (s), 187.2 (s), 210.0 (s).

Pyrolysis of the thiocarbonate (1.0 g) was effected at 200 °C under reduced pressure (0.1 torr) in a evacuated apparatus consisting of a 25-mL round-bottom flask connected to an U-shaped tube cooled to −70 °C. The product was taken into ether and the organic layer washed with 2 N NaOH solution and brine and dried. Flash chromatography of the crude product afforded 450 mg (80% from 9) of pure olefin 11: sublimation at 80–90° (1 torr); mp (sealed tube) 140–141 °C; IR 1720, 3040 cm^{-1}; ^1H NMR δ 1.13 (s, 3 H), 1.26 (s, 3 H), 5.53 (m, 2 H); ^{13}C NMR δ 26.0 (q), 26.5 (q), 31.8 (t), 39.2 (d), 41.5 (s), 42.2 (t), 46.4 (t), 124.0 (d), 131.2 (d), 211.9 (s). Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.83. Found: C, 80.02; H, 9.84.

B. From 4. To a stirred solution of LDA (prepared by adding 4 mL (6.4 mmol) of 1.6 M *n*-BuLi solution in hexane to a solution of 0.9 mL (6.4 mmol) of diisopropylamine in 8 mL of THF) at −70 °C under argon atmosphere was added a solution of the ketone 4 (1.35 g, 6 mmol) in THF (15 mL). The mixture was stirred at −70 °C for 45 min and diethyl chlorophosphate (1.7 mL, 12 mmol) was added. Stirring was continued at room temperature for 2.5 h. The yellow reaction mixture was diluted with ether and poured into ice-cold saturated $NaHCO_3$ and the product was extracted with ether. The combined organic layers were washed with ice-cold 1.2 M HCl. The crude product was dissolved in wet benzene and refluxed with 100 mg of *p*-TSA for 2 h. Extraction with ether and the usual workup yielded a crude product which was purified by flash chromatography giving 1.52 g of 10 as a yellow oily product: IR 1270, 1680, 1712, 2910 cm^{-1}; ^1H NMR δ 1.16–1.41 (several pics, 12 H), 4.08 (d, q, 4 H), 5.43 (m, 1 H); ^{13}C NMR δ 15.9 (q), 16.3 (q), 25.8 (q, 2 C), 32.1 (s), 32.9 (t), 39.3 (d), 40.3 (d), 42.2 (t), 46.1 (t), 64.5 (t, 2 C), 114.5 (d), 145.8 (s), 210.1 (s).

Reduction of 10 by Lithium Ethylamide. A solution of 1.52 g of enol diethyl phosphate in 3 mL of THF and 1.1 mL of *t*-BuOH was added dropwise over a period of 1 h to a stirred solution of lithium (0.6 g) in ethylamine (50 mL) at 0 °C under argon. The reaction mixture was stirred for an additional 2 h at room temperature and then quenched by slow addition of water. The aqueous mixture was neutralized with dilute HCl solution in order to dissolve the lithium hydroxide. Extraction with ether and the usual workup yielded 824 mg of crude product which gave after flash chromatography 500 mg. The substance is identical with 11 as prepared above.

9,9-Dimethylbicyclo[3.3.1]non-6-en-3-*exo*-ol (13). To a stirred solution of 11 (226 mg) in absolute ethanol (8 mL) was added 0.7 g of sodium under argon atmosphere. The mixture was refluxed for 45 min, cooled, and poured into water. Extraction with ether and the usual workup yielded 233 mg of oily product which gave after flash chromatography 215 mg of colorless crystallized 3-exo-ol 13. Recrystallization from aqueous methanol: mp 107–108 °C; IR 1045, 1170 and 3600 cm^{-1}; ^1H NMR δ 0.98 (s, 3 H), 1.1 (s, 3 H), 4.0 (m, 1 H), 5.61 (m, 2 H); ^{13}C NMR δ 26.3 (q), 26.6 (q), 31.9 (s), 33.2 (t), 37.9 (s), 39.3 (t), 40.8 (d), 65.4 (d), 127.3 (d), 130.0 (d).

Reduction of 11 with $LiAlH_4$. To a stirred suspension of $LiAlH_4$ (0.2 g) in dry ether (7 mL) was added 315 mg of ketone 11 in ether (10 mL) under argon atmosphere. The mixture was refluxed for 2 h and cooled in an ice–water bath, and excess of hydride was destroyed by dropwise addition of 5% HCl solution. Extraction with ether and the usual workup yielded 326 mg of crude product as a mixture of epimeric alcohols 13 and 14. Separation by flash chromatography afforded 163 mg of the endo alcohol 14: sublimation at 80–90 °C (1 torr) gave colorless crystals; mp (sealed tube) 65 °C dec; IR 3550 cm^{-1}; ^1H NMR δ 1.00 (s, 6 H)8 3.85 (m, 1 H), 5.83 (m, 2 H); ^{13}C NMR δ 26.0 (q), 27.1 (q), 31.7 (s), 31.9 (t), 33.0 (t), 27.1 (t), 38.6 (d), 65.8 (d), 127.1 (d), 13.9 (d). Anal. Calcd for $C_{11}H_{20}O$: C, 79.46; H, 10.92. Found: C, 79.82; H, 10.40.

Further elution gave 140 mg of the exo epimer identical with 13 as prepared above.

9,9-Dimethylbicyclo[3.3.1]nonan-3-*exo*-ol (15). A solution of 100 mg of 13 in 7 mL of EtOH was stirred with 10% palladium on activated charcoal under hydrogen atmosphere for 30 min.

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Filtration and evaporation of the solvent gave 90 mg of **15** as a colorless crystallization product: sublimation at 80–90 °C (1 torr); mp (sealed tube) 134–135 °C; IR 3630 cm^{-1}; ^1H NMR δ 1.00 (s, 3 H), 1.06 (s, 3 H), 2.53 (s, 1 H), 4.33 (sept, 1 H).

9,9-Dimethylbicyclo[3.3.1]nonan-3-*endo*-ol (16). The hydrogenation of **14** was achieved by stirring the reaction mixture under hydrogen atmosphere for 14 h. Usual workup and recrystallization from aqueous methanol afforded colorless needles: mp 41 °C dec; IR 3600 cm^{-1}; ^1H NMR δ 0.88 (s, 3 H), 1.00 (s, 3 H), 4.08 (m, 1 H).

9,9-Dimethylbicyclo[3.3.1]nonan-3-one (12). Hydrogenation of 165 mg of **11** in the same conditions gave 160 mg of saturated ketone **12** as oily product which crystallized slowly on cooling: sublimation at 80–90 °C (1 torr); mp 73–75 °C; IR 1715 cm^{-1}; ^1H NMR δ 1.16 (s, 6 H).

9,9-Dimethylbicyclo[3.3.1]nonan-3-one Ethylene Acetal (17). A mixture of 100 mg of **12**, 10 mL of benzene, 10 mg of *p*-TSA, and 0.1 mL of 1,2-ethanediol was refluxed for 6 h. The usual workup gave 140 mg of crude product as a mixture of **17** along with the starting material. Separation by flash chromatography yielded 77 mg of **17** as a colorless oil: IR 1095 cm^{-1}; ^1H NMR δ 1.05 (s, 6 H), 3.56 (m, 4 H). **12** (21 mg) was obtained as colorless crystals.

9,9-Dimethylbicyclo[3.3.1]nonane-3,7-dione (5). A solution of the Michael adduct **3** (2.2 g) and NaOH (2.0 g) in methanol (50 mL) and water (50 mL) was refluxed overnight under argon, cooled, and acidified with 10% aqueous HCl. The aqueous solution was extracted with ethyl acetate to yield 1.25 g of white solid product. Recrystallization from ether gave **5** as colorless crystals: mp 127–128 °C; IR 1710 cm^{-1}; ^1H NMR δ 1.40 (s, 6 H); ^{13}C NMR δ 26.2 (q), 32.7 (s), 41.2 (d), 45.1 (t), 208.7 (s). Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.05; H, 8.80.

Sodium Borohydride Reduction of the Diketone 5. The Hemiacetal 6. Sodium borohydride (18 mg, 0.45 mmol) was added to a stirred solution of the diketone **5** (320 mg, 1.78 mmol) in 95% ethanol (5 mL). After 20 min, water (1 mL) was added and the mixture refluxed gently for 15 min. More water was added, and the solution extracted with ether, which was then dried and evaporated. Flash chromatography of the crude product gave 200 mg of the hemiacetal **6** which crystallized from pentane–ether: mp (sealed tube) 192–193 °C; IR 3600, 1190 cm^{-1}; ^1H NMR δ 1.10 (s, 6 H), 4.23 (m, 1 H), 4.35 (s, 1 H). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.12; H, 9.64.

Registry No. **1**, 1073-14-9; **2**, 1830-54-2; **3** (isomer 1), 94519-31-0; **3** (isomer 2), 94519-32-1; **3** (7-ketal), 94519-43-4; **4**, 37741-10-9; **5**, 37741-08-5; **6**, 94519-33-2; **7**, 94519-34-3; **8**, 94519-35-4; **9**, 94519-36-5; **9** (thiocarbonate), 94519-44-5; **10**, 94519-37-6; **10** (ketal), 94519-45-6; **11**, 94519-38-7; **12**, 75984-11-1; **13**, 94519-39-8; **14**, 94519-40-1; **15**, 75984-06-4; **16**, 75984-16-6; **17**, 94519-41-2; **18**, 75984-22-4; **19**, 94519-42-3; 1,2-ethanediol, 107-21-1; *p*-tolyl chlorothioformate, 937-63-3; diethyl chlorophosphate, 814-49-3.

Substituent Effects on ^{13}C NMR Chemical Shifts and One-Bond ^{13}C–^{13}C Coupling Constants in 1- and 4-Substituted Diamantanes

V. V. Krishnamurthy, Joseph G. Shih, and George A. Olah*

Donald P. and Katherine B. Loker Hydrocarbon Research Institute and Department of Chemistry, University of Southern California, Los Angeles, California 90089

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One-bond ^{13}C–^{13}C NMR coupling constants in a series of 1- and 4-substituted diamantanes were measured at natural abundance by using the INADEQUATE pulse sequence. The substituent effect on ^{13}C chemical shifts (SCS) and ^{13}C–^{13}C coupling constants (SCC) was analyzed in terms of the electronegativity and steric effects of the substituents and in terms of the number and type of the gauche interaction. The trends observed in the C_α–C_β, C_β–$C_{\gamma_{anti}}$, and C_β–$C_{\gamma_{syn}}$ coupling constants are in accord with results obtained on 1- and 2-substituted adamantanes.

Recent advances in instrumentation and the availability of high-field NMR spectrometers have greatly increased the scope and utility of ^{13}C–^{13}C NMR coupling constants in structural studies. While recent theoretical studies[1,2] have reproduced certain qualitative trends in experimental values, they are still far from giving quantiative agreements. Thus, there has been considerable effort to obtain more extensive experimental values of J_{CC}[3-6] and to find empirical correlations with other molecular properties which are dependent on the same electronic characteristic of the molecules.

The basic problem in observing the ^{13}C–^{13}C coupling constants in the NMR spectra of compounds with natural abundance ^{13}C is that of identifying the appropriate weak satellite signals on the sides of strong ^{13}C lines. The INADEQUATE pulse sequence technique developed by Freeman et al.[7] enables one to investigate one-bond and long-range carbon–carbon couplings by suppressing the strong signals from molecules with isolated ^{13}C nucleus.

Although substituent effects on J_{CC} values have been studied[2,8,9] to some extent, mostly with ^{13}C-labeled compounds, studies of stereochemical effects on J_{CC} values

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